α/β or TD_{50} in normal tissue by immunological aspects was expected to improve normal tissue response in radiotherapy. For more precise prediction of such optimal protocols, treatment planning systems should be incorporated the biological optimization in clinical practice.

Keywords: Immuno-radiotherapy, normal tissue response, NTCP

References:

[1] S.C. Formenti, S. Demaria. Combining radiotherapy and cancer immunotherapy: a paradigm shift. J Natl Cancer Inst. 105(4):256-65, 2013.
[2] P.G. Prasanna, H.B. Stone, R.S. Wong et al. Normal tissue protection for improving radiotherapy: Where are the Gaps? Transl Cancer Res. 1(1):35-48, 2012.
[3] R. G. Dale, B Jones. Radiobiological Modelling in Radiation Oncology. British Inst of Radiology, 2007.

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Current Status of particle therapy at CNAO

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The Italian Center for Oncologic Hadrontherapy is up to date in the fifth year of its clinical activity. The total number of patients treated is 685 (up to November 2015). The treatments with carbon ions are about three times those with protons. An important part of treatments with carbon ions is directed on sarcomas, bones and soft tissue sarcomas, salivary glands tumours. In the table, treated patients are listed according to the clinical trials approved by the Italian Ministry of Health.
Another substantial part of treatments regards re-irradiation of several pathologies, especially head and neck re-treatments of several tumours.
An important goal reached in the last year is the treatment of moving targets. Pancreatic adenocarcinomas, hepatocellar carcinomas and pathologies located in moving sites are treated through the vertical beam line with gating and rescanning technology.
Treated volumes' issue has been discussed. Many pelvic sarcomas and chordomas cases refer to hadrontherapy treatment when already reached remarkable volumes. These cases are subject of discussion amongst radiation oncologists and medical physicists. The parameters taken in consideration are PTV (Planning Treatment Volume) and GTV (Gross Tumour Volume). They are statistically evaluated to elaborate the best treatment strategy in term of dose and planning option. This issue has also economic implications. The treatment of major tumour volumes using mostly more than one field occupies the treatment room for a period of time equal, when not superior, to two or more patients. The next challenge is to improve all steps to give such treatments in less time.
Most of the patients treated at CNAO are referred from Italian Cancer institutes but an increasing number of EU patients comes to Pavia through international agreements.
In the coming period CNAO is expected to receive the authorization to treat all the clinical case worth to receive hadrontherapy treatment.

Clinical study description	Particle	Total number of patients treated
Proton radiation therapy for chordomas and chondrosarcomas of the skull base	Protons	52
Proton therapy of spine chordoma and chondrosarcoma (amended)	Protons	16
Proton therapy of intracranial meningioma	Protons	24
Proton therapy of brain tumors	Protons	11
Proton therapy of recurrent cervico-cephalic area tumors	Protons	21
Proton boost for locally advanced cervico-cephalic area tumors	Protons	28
Proton therapy of glioblastoma	Protons	1
Proton re-irradiation of recurrent spine chordoma and	Protons	6
Carbon ion therapy of adenoid cystic carcinoma of salivary glands	Carbon ions	106
Carbon ion re-irradiation of recurrent pleomorphic adenomas	Carbon ions	19
Carbon ion re-irradiation of recurrent rectal cancer	Carbon ions	8
Carbon ion radiotherapy for bone and soft tissue sarcoma of cervico-cephalic area	Carbon ions	94
Carbon ion radiotherapy for bone and soft tissue sarcoma of trunk	Carbon ions	119
Carbon ion therapy of recurrent cervico-cephalic area tumors	Carbon ions	90
Carbon ion therapy of malignant melanoma of the mucous of the upper aerodigestive tract	Carbon ions	14
Carbon ion therapy for high risk prostate cancer	Carbon ions	9
Carbon ion therapy of primary and secondary orbital tumors	Carbon ions	13
Carbon ion therapy for pancreatic cancers	Carbon ions	11
Carbon ions therapy of primary malignant tumors of the liver	Carbon ions	4
Carbon ion re-irradiation of recurrent spinal chordoma and	Carbon ions	7
Protons and/or carbon ion integrated radiotherapy for poor prognosis in patients with inoperable sinonasal tumor	Protons/ Carbon ions	4
Other	-	28
		685

Keywords: carbon ions, gating, volumes.

References:

[1] Giordanengo S, Garella MA, Marchetto F, et al. The CNAO dose delivery system for modulated scanning ion beam radiotherapy. Med Phys. 2015 Jan;42(1:263-75.
[2] Via R, Fassi A, Fattori G, et al. Optical eye tracking system for real-time noninvasive tumor localization in external beam radiotherapy. Med Phys. 2015 May;42(5):2194.

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Molecular imaging for theranostics

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Molecular imaging provides unique information on the tumor phenotype (i.e. tumor cells and tumor microenvironment), influencing treatment decisions and adaptation of therapy by early prediction of treatment outcome. With the increasing importance of systemic targeted therapies and of high precision external beam radiotherapy, interrogating tumor characteristics before and during therapy becomes increasingly important.
Key features like tumor metabolism, proliferation and protein synthesis can be depicted by the well-known radiopharmaceuticals FDG, FLT and e.g. FAZA, respectively. Furthermore, imaging receptor expression on tumor cells with e.g. radiolabeled antibodies and peptides can provide information on the presence, heterogeneity, accessibility, and modulation of these receptors for targeted therapies. Thirdly, small molecules like TKI may radiolabeled providing similar insight in tumor pathophysiology allowing better selection of patients likely to respond to treatment. A distinct form of theranostics utilizes targeting molecules, radiolabeled with an gamma or positron emission for imaging selecting patients for treatment with the same molecule, now radiolabeled with a beta-emitter.
In conclusion, various applications of theranostics provide crucial insight in tumor biology, the choice and adaptation of treatment, allowing better selection of treatment to achieve better outcomes for cancer patients.

Keywords: molecular imaging, theranostics, radiopharmaceuticals

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Comparative evaluation of the in vitro the comet assay for the detection of genotoxic effects of 60 MeV protons and X-ray radiation

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The aim of the study was to investigate the biological effects in human lymphocytes irradiated with the 60 MeV proton beam in the Bronowice Cyclotron Center IFJ PAN. The relative biological effectiveness (RBE) of the proton beam in comparison to X-ray's was estimated by the comet method.
Whole blood samples were collected from 5 healthy donors. For dose-response studies lymphocytes were used submerged in agarose on microscopic slides, set in a specially designed PMMA phantom located at the isocenter. Cells were irradiated in Eppendorf vessels located in the mead of Spread-Out Bragg Peak (SOBP) in the fully modulated proton beam with range of 29 mm.
For reference, the lymphocytes were exposed to the 250 kV X-rays. For both sources of radiations, dose-effect curves at a dose range (0-4Gy) were estimated. The level of DNA damage was assessed using the alkaline version of comet assay, also called the DNA single cell gel electrophoresis (SCGE).
The obtained dose-response relationships for the level of DNA damage showed linear character for both sources of radiation (R^2 = 0.994 for protons and R^2 = 0.995 for X-rays). The efficiency of protons in inducing DNA strand breaks for the dose range from 0.3 to 4 Gy calculated as the ratio of the two α coefficients was 1.37. The average RBE calculated from the proton and X-ray dose required for the iso-effective TDNA comet assay parameter was 1.51 + / - 0.05 (range 1.45-1.66).
This observation suggests that the standard alkaline comet assay is reliable technique for estimation of DNA damage caused by proton and X-ray radiation *in vitro*.

Keywords: Proton beam, Human lymphocytes, DNA damage

Note: These investigations were partially supported by grant DEC-2013/09/D/NZ7/00324 from the National Science Centre, Poland.

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The project of radio-isotope complex RIC-80 at PNPI
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Presently for production of medical radionuclides the cyclotrons are widely used which are very safe and reliable installations. At PNPI a high current cyclotron C-80 with the energy of extracted proton beam of 40-80 MeV and the current up to 200 μA has been constructed. One of the main goals of C-80 is production of a wide spectrum of medical radio-nuclides for diagnostics and therapy. At the beam of C-80 the project of radioisotope complex RIC-80 (Radio Isotopes at the cyclotron C-80) has been worked out. In the presented submission the project of RIC-80 complex is discussed, which includes three target stations for production of radio-nuclides for medicine. The peculiarity of the proposed radio-isotope facility is the use of the mass-separator with the target-ion source device as one of the target stations for on-line, or semi on-line production of a high purity separated radio-nuclides. The results on the target development for production of radio-isotope generator for PET diagnostics ^{82}Sr are presented.

Keywords: Radioisotopes for medicine, mass-separator, targets for radioisotope production

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Fused Toes Homolog (FTS) regulates EGF-induced epithelial–mesenchymal transition (EMT) and migration of cervical cancer cells
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Purpose: Epithelial–mesenchymal transition (EMT) allows tumor cells to acquire the capacity to infiltrate surrounding tissue and to ultimately metastasize to distant sites. Limited information is available on the regulation of EMT in cervical cancer. Epidermal growth factor (EGF) has beenreported as a potent stimulator of cervical cancer invasiveness. Upregulation of epidermal growth factor receptor (EGFR) expression is reported in the recurrent cervical cancer. Fused Toes Homolog (FTS) has been reported as a general regulator of AKT activity in the control of differentiation, proliferation, and apoptosis in many cell types. Importantly, studies from our laboratory have shown overexpression of FTS in cervical cancer specimens and the expression of this protein increases with advancement of the disease. Hence, we studied the role of FTS in EGF-induced EMT in cervical cancer cells.
Materials and Methods: A human cervical carcinoma cell line ME180 was used. Gene silencing was obtained using siRNA. Protein expression was studied by Western blot and immunofluorescence. Cell migration and invasion was assessed by wound healing and matrigel migration assay.
Results: EGF treatment induced the change of EMT markers and increased cell migration. EGF treatment also increased phosphorylated EGFR and ERK and nuclear level of ATF-2. The binding of ATF-2 to the promoter region of FTS was evidenced after EGF treatment. Pretreatment with PD98059 and gefitinib prevented EGF-induced FTS expression. FTS-silencing reduced EMT and cell migration by EGF treatment.
Conclusions: These results suggest that upregulation of FTS by EGF is mediated via EGF/EGFR/ERK/ATF-2 and this facilitates EGF-mediated EMT process in cervical cancer cells. FTS can be a potential target to circumvent cervical cancer progression driven by EGF.

Keywords: Fused Toes Homolog (FTS), Cervix cancer, Epithelial–mesenchymal transition (EMT)

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Tuning of a 4D ML reconstruction strategy for treatment verification in ion beam radiotherapy
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Purpose: In PET-based treatment verification the low counting statistics PET data acquired during/after the treatment (Measured PET) must be compared to a Monte Carlo estimate of the β+ distribution induced by the treatment (Expected PET) based on the planning Computed Tomography (CT) images [1]. Given the extremely low quality of Measured PET images and the consequent difficulties in mismatch estimation, we proposed to use a 4D Maximum Likelihood (ML) reconstruction strategy considering Expected PET and Measured PET as two frames of a 4D dataset and providing an estimate of the motion field mapping one frame to the other [2].
The aim of this work is to optimize the strategy on a